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EXAMINER	
MAYER, SUZANNE MARIE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 05/25/2004

Restart

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,245	NELSON ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

Content of the entire specification is objected to.

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words but may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(e) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to

specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(h) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(j) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international

application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(k) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

The specification is also objected as the name 'Karposi' should be 'Kaposi' and is misspelled through out.

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is rejected for failing to properly identify correctly the invention which is it claiming. The name 'Karposi' should be 'Kaposi'. This same misspelling occurs throughout the specification.

Claim 9 provides for the use of a peptide that is permeable to a cell membrane that delivers a molecule intracellularly, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending

to encompass. Claim 10 provides for the use of a peptide that is permeable to a cell membrane that delivers peptide nucleic acids to *in vivo* targets, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 9 and 10 are also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The instant claims read on 'analogues' of cell permeable signal peptides as stated in Claims 1, 6 and 8. Thus, the claims read on any type of analogue of a signal

peptide. The specification, however, does not provide any type of explanation as to what an analogue of a cell permeable signal peptide actually is. A cell permeable signal peptide analogue could have several different meanings. For example, the following examples all meet the definition of analogues of cell permeable signal peptides: i) the addition of a single amino acid to a cell permeable signal peptide, ii) the addition of 20 amino acids to a cell permeable signal peptide or iii) the use of alternative amino acids (e.g. seleno-methionine) to a cell permeable signal peptide, just to name a few. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of cell permeable signal peptide analogues by any identifying structural characteristics or properties, for which no predictability of structure is apparent. Given the breadth of what an analogue of a cell permeable peptide could encompass as indicated in the claims, Applicants written description of the claimed invention is insufficient to show that the Applicants were in possession of the full scope of the claimed invention.

Claims 1,6 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims read on 'analogues' of a signal peptide as stated in Claims 1, 6 and 8. Thus, the claims read on any type of analogue of a signal peptide. The scope

of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art. The instant specification is not enabling for claims drawn to analogues of cell permeable peptides.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary is great, (2) the amount or direction or guidance presented in the specification is insufficient and non-existant, (3) the presence of working examples is not present in the specification, (4) the nature of the invention of how to use analogues is unclear, (5) the state of the prior art does not readily teach the invention in the claims, (6) the relative skill of those in the art to reproduce the invention is high, (7) the predictability or unpredictability of the art is high, and (8) the breadth of the claims are very broad.

The instant specification is not enabling for claims drawn to analogues of cell permeable signal peptides. An analogue could encompass a broad range meanings or different experiments. As stated above, a signal peptide analogue could mean the addition of a single amino acid or the use of amino acid analogues such as hydroxyl-lysine, seleno-methionine etc., or the addition of any N amino acids to the signal peptide where N is equal to *any* number. It is not clear from the specification how one skilled in the art would be able to reproduce the invention as stated in the claims with out undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (in The Journal of Biological Chemistry, "Inhibition of Nuclear Translocation of Transcription Factor NF-κB by a Synthetic Peptide Containing a Cell Membrane-permeable Motif and Nuclear Localization Sequence, 1995, 270(24), pp. 14255-58).

Lin et al. teach a cell permeable peptide comprised of a hydrophobic core of a synthetic signal peptide at Figure 1, p.14256, second column, and p14526 1st column, last paragraph, where the hydrophobic region of Kaposi fibroblast growth factor (K-FGF) signal peptide sequence was used as the core of the signal peptide with four

different variations of peptides being produced. Therefor, Claims 1 and 2 are rejected over Lin et al.

Claim 3 is rejected over Lin et al. Claim 3 claims a cell permeable peptide as in claims 1 and 2 wherein at least one positively charged amino acid is chosen from lysine and/or arginine and a positively charged analogue thereof. Since Lin et al. teach a cell permeable peptide of sequence SN50 (AAVALLPAVLLALLAPVQRKRQKLM) (see Figure 1, p. 14256) which possesses two lysine residues, then this is sufficient to anticipate this claim.

Claims 4 and 5 are also rejected over Lin et al., since we are taught of a modified a cell permeable peptide is an analogue of K-FGF and has more than one lysine (see Figure 1, sequence SN50, p. 14256).

Claim 7 is rejected since the claim is directed to a cell permeable peptide, as in any of claim 1 to 6 which contains multiple positively charged amino acids or analogues thereof, wherein a peptide nucleic acid *may be* conjugated to each positively charged residue and wherein the peptide nucleic acids conjugated by such means are identical or different. The examiner understands this claim to read that the cell permeable peptides *may be conjugated but does not necessarily have to be conjugated* to each positively charged residue and therefor this claim would also be anticipated by Lin et al., as we are taught of a cell permeable peptide with multiple charged amino acids.

Claim 8 is rejected since it is directed to a cell permeable peptide, as in claims 1-6, that comprises at least one positively charged amino acid residue or functionally

equivalent positively charged analogue thereof, conjugated or *conjugatable* to a lysine tree, to which multiple peptide nucleic acids may be joined for transport and presentation of multiple peptide nucleic acids. The examiner rejects this claim as the use of the alternative when considering a cell permeable peptide that 'is conjugated or conjugatable' which infers that a cell permeable peptide may be, but does not necessarily have to be conjugated to a lysine tree or anything else and subsequently the claim is simply claiming a cell permeable peptide as in claims 1-5, 7 which have already been rejected over Lin et al.

Claim 9 is rejected because Lin et al. teach of a cell permeable peptide that is capable of intracellular delivery of radio-labeled Iodine (^{125}I) to the nucleus of a cell by using a cell permeable signal peptide SKP (see p. 14255, 2nd col., 3 paragraph, and sequence on p. 14256, Figure 1). The examiner in this case views the radio labeled iodine and the SPK signal peptide as being a molecule.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 6 is rejected under 35 U.S.C. 103(a) as obvious in view of Dokka et al. (in Pharmaceutical Research, "Cellular Delivery of Oligonucleotides by Synthetic Import

Peptide Carrier", 1997, 14(12), pp. 1759-64). Claim 6 claims a cell permeable peptide as claimed in claim 5 wherein one or more lysine residues are attached to the C-terminal of the signal sequence peptide or signal sequence peptide analogue. Dokka et al. teach a poly-L-lysine tail comprising 10 lysine residues but neglect to intimate which terminus of the signal peptide it is attached too. It therefor would have been obvious to one of ordinary skill in the art at the time the invention was made to either attach the additional lysine residues to the C-terminus or just or N-terminus of the signal peptide because it is well known in the art that the such polycationic tails aid in facilitating transport of cell permeable peptides across various types of cell membranes.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Suzanne M. Mayer whose telephone number is 571-272-2924. The examiner can normally be reached Monday to Friday from 9am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
May 11, 2004

ROBERT A. WAX
PRIMARY EXAMINER